# Assesment of The Efficacy of Thyroid Function Screening in Early Pregnancy

# Erken Gebelikte Tiroid Fonksiyonlarının Taranmasının Etkinliğinin Değerlendirilmesi

Gebelikte Tiroid Fonksiyonlarının Taranması / Thyroid Function Screening in Pregnancy

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**Özet**

Amaç: Çalışmamızda, erken dönem gebelikte tiroit fonksiyonlarının taranmasının etkinliğini değerlendirmeyi amaçladık. Gereç ve Yöntem: Çalışmamıza, ikincil bir merkeze ilk gebelik vizitleri için (6-12 gebelik haftası) Mayıs 2012 ile Ağustos 2012 tarihleri arasında başvuran 185 gebe dahil edildi. Hastalar risk faktörlerine göre iki gruba ayrıldı: 94 kişi yüksek riskli, 91 kişi düşük riskli olarak kabul edildi. Maternal serumda tiroit stimüle edici hormon (TSH), serbest tiroksin (sT4), serbest tri-iyodotironin (sT3) ölçüldü. Ölçüm sonucuna göre, hasta grubu; ötiroit, hipertiroit, hipotiroit, subklinik hipotiroit ve subklinik hipertiroit olarak gruplandırıldı. Verilerin analizi SPSS for Windows 11.5 programı ile yapıldı. Tüm testlerde, p< 0.05 için sonuçlar istatistiksel olarak anlamlı kabul edildi. Bulgular: Çalışmamızda, 185 gebeden, 151 gebe (%81,62) ötiroit iken, 34 gebede (%18.38) tiroit disfonksiyonu tespit edildi. Bunlardan 24'ü (%12,98) yüksek riskli grupta, 10'u (%5,4) ise düşük riskli gruptaydı. Tiroit fonksiyonları normal ve anormal olarak değerlendirildiğinde, anormal test sonunda istatistiksel olarak en anlamlı olan karakteristik özellikler, antitiroit tedavi almış olmak ve tiroit cerrahisi geçirmiş olmaktı. (p=0.005, p=0.015) Çalışmamızda yalnız yüksek riskli gebeleri taramış olsaydık, disfonksiyonların yaklaşık üçte birini tespit edemeyeceğimizi saptadık. Tartışma: Gebeliğin erken döneminde sadece risk faktörleri esas alınarak maternal tiroit fonksiyonlarının taranması, tiroit bozukluklarının atlanmasına yol açabilir. Fakat, üniversal mi yoksa risk faktörü hedefli taramanın mı olması gerektiği konusundaki tartışma gelecekte de sürmeye devam edecek gibi görünmektedir.

**Anahtar Kelimeler**

Hipertiroidi; Hipotiroidi; Gebelik; Tarama; Tiroit Disfonksiyonu

**Abstract**

Aim: To asses the efficacy of screening thyroid function during early pregnancy. Material and Method: One hundred and eighty five pregnant women who attended a secondary center for their first antenatal visits (6-12 weeks of gestation) between May 2012 and August 2012 were divided into two groups comprising 94 women regarded as high-risk and 91 low-risk. Maternal serum concentrations of TSH, fT4 and fT3 were measured. The thyroid function of the study group was evaluated for euthyroidism, hypothyroidism, hyperthyroidism, subclinical hypothyroidism, and subclinical hyperthyroidism according to TSH, fT3 and fT4 results. Analysis of data were performed, using the SPSS software version 11.5. In all tests, p<0.05 was accepted as statistically significant. Results: We screened thyroid function in 185 pregnant women, of whom 151 (81.62%) were euthyroid and 34 (18.38%) had thyroid dysfunction, with 24 (12.98%) in the high-risk group and 10 (5.4%) in the low-risk group. When the results of thyroid function tests were evaluated as normal and abnormal, the most statistically significant characteristics for abnormal results were found to be history of antithyroid therapy and thyroid surgery (p=0.005, p=0.015). We would fail to spot about one third of thyroid dysfunctions if only high-risk women were screened. Discussion: Risk-stratified screening for maternal thyroid dysfunction during early pregnancy may led to neglected diagnoses of thyroid disorders. Results here indicated universal screening, but the debate regarding the targeting of high-risk cases seems set to continue into the future.

**Keywords**

Hyperthyroidism; Hypothyroidism; Pregnancy; Screening; Thyroid Dysfunction

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## Introduction

Thyroid disease is the second most common endocrine dysfunction among women of childbearing age [1]. While hyperthyroidism affects 0.2% of pregnant women, 95% of these have a diagnosis of Graves' disease, it affects 2.5% of pregnant women [2-4]. Both hyperthyroidism and Graves' disease have maternal and fetal risks during pregnancy. The adverse outcomes of hyperthyroidism, which is predominantly linked causally with circulating thyroid peroxidase autoantibodies, are miscarriage, growth restriction, premature labor, placental abruption, pregnancy induced hypertension, preeclampsia, gestational diabetes, infection, cesarean delivery, congenital malformation, and increased perinatal mortality; [5-10]; it is also associated with impaired neuropsychiatric development and cretinism in the offspring of affected mothers [11].

Because of all these adverse outcomes of thyroid dysfunction during pregnancy, it is extremely important to diagnose and treat the disease timely. However, diagnosis and management can be difficult because of the physiologic changes in the levels of pituitary and thyroid hormones during pregnancy. Also, determination of the gestational age specific reference intervals for thyroid-stimulating hormone (TSH), free thyroxine (fT4), and free tri-iodothyronine (fT3) in each region are also essential to avoid misdiagnosis [12-14].

Despite the possible subsequent adverse outcomes of thyroid disease in pregnancy, universal screening of thyroid function in early pregnancy is not generally advocated owing to the lack of evidence based practice. However, there have been some restrictions to find out new evidences in many stuides, such as high costs and issue bias. [27] As a result, The American Thyroid Association, American Association of Clinical Endocrinologists and Endocrine Society all recommend screening only high-risk pregnant women [15;16]. The results of several studies, however, suggest that all pregnant women should be screened [17-21]. In the current study, we aimed to evaluate the efficacy of thyroid function screening for all pregnant women in a secondary setting during early pregnancy.

## Material and Method

The study comprised 185 pregnant women attending Konya Eregli State Hospital outpatient obstetric clinic for their first antenatal visits (6-12 weeks of gestation) between May 2012 and August 2012. Duration of gestation was calculated from the last menstrual period and verified by ultrasonography. Subjects were asked for personal and family history to determine the high-risk group. High-risk indicators for thyroid dysfunction were a history of thyroid dysfunction and/or surgery, miscarriage or preterm delivery, autoimmune disorders, infertility, receiving radiation to head and neck, being treated with antithyroid drugs, amiodarone or lithium, having goiter or type 1 diabetes mellitus, age 30 years or older, and being morbidly obese (Body mass index>30) . Subjects were then divided into two groups, 94 determined as high-risk and 91 low-risk. [15]

Serum concentrations of TSH, fT4 and fT3 were measured by the fully automated electrochemiluminescent immunoassay, run on the Siemens Advia CP analyzer. The reference ranges for TSH,fT4 and fT3 were 0.27-4.2 mIU/liter, 12-23 pmol/liter, and 4-7.8 pmol/liter for the first trimester. [16] The thyroid function of the study group was evaluated as euthyroidism, hypothyroidism, hyperthyroidism, subclinical hypothyroidism(decreased fT4 and fT3 levels with normal TSH) and subclinical hyperthyroidism(elevated fT4 and fT3 levels with normal TSH) according to TSH, fT3 and fT4 results.

The study was approved by the local research ethics committee and written informed consent was obtained from each subject. Data were analyzed using the SPSS for Windows version 11.5 software. The distribution of continuous variables was examined by the Shapiro Wilk test. Descriptive variables were indicated as average, standard deviation or median (minimum and maximum) for continuous variables. The nominal variables were indicated as case numbers and percentages. Statistical significance across the groups was evaluated by student's t-test for the mean and the Mann Whitney U test for the median values. Nominal variables were examined by chi-square or Fisher's Exact test. In all tests, $p<0.05$ was accepted as statistically significant.

## Results

We screened thyroid function in 185 pregnant women. The subjects were divided into two groups: 91 were determined as low risk and 94 as high risk. Comparisons of demographic data are shown in table 1. High-risk pregnancies were significantly older, more parous, and had more prior miscarriages (Table1).

Among the 185 pregnant women, 151 (81.62%) were euthyroid and 34 (18.38%) had thyroid dysfunction, 24 (12.98%) of whom were in the high-risk group and 10 (5.4%) in the low-risk group (Table 2). There were 14(14.9%) subclinical hyperthyroid women in high-risk group and no subclinical hypothyroid woman was

Table 1. Demographic characteristics of pregnant women (n=185)

| Characteristics | Low-risk group (n:91) | High-risk group (n:94) | P value |
|---|---|---|---|
| Age (years) | 24.1±3.6 | 30.4±5.8 | <0.001 |
| Gravida | 2 (1-5) | 2 (0-9) | <0.001 |
| Parity | 1 (0-4) | 1 (0-8) | <0.001 |
| No. of prior miscarriages | 0 (0-1) | 0 (0-4) | <0.001 |
| Gestational age(week) | 9 (5-12) | 9 (5-15.7) | 0.752 |
| Smoking | - | 6 (6.4%) | - |
| TSH(mIU/liter) | 0.98 (0.03-15) | 0.80 (0.01-49) | 0.319 |
| fT3 (pmol/liter) | 4.7 (3.5-5.8) | 4.6 (2.3-6.0) | 0.582 |
| fT4(pmol/liter) | 10 (5.1-25) | 10 (3.8-24) | 0.708 |
| History of antithyroid therapy | - | 11 (11.7%) | <0.001 |
| History of thyroid surgery | - | 3 (3.2%) | 0.246 |
| Family history of thyroid disease | - | 28 (29.8%) | <0.001 |
| History of either autoimmune disease | - | 1 (1.1%) | - |

TSH: Thyroid-stimulating hormone, fT3: free thyroxine (fT4), fT3: free tri-iodothyronine

Table 2. Distribution of thyroid function in risk groups

| Result | Low-risk group (n=91) | High-risk group (n=94) | p-value |
|---|---|---|---|
| Euthyroidism | 81 (%89,0) | 70 (%74,5) | 0,011 |
| Hypothyroidism | 3 (%3,3) | 7 (%7,4) | 0,331 |
| Hyperthyroidism | 2 (%2,2) | 1 (%1,1) | 0,617 |
| Subclinical hypothyroidism | - | 2 (%2,1) | 0,497 |
| Subclinical hyperthyroidism | 5 | 14 (%14,9) | 0,035 |

Table 3. Distribution of thyroid function according to study group demographic characteristics

| Characteristics | Normal (n:70) | Abnormal (n:24) | P value |
|---|---|---|---|
| Age | 30.7±5.9 | 29.4±5.6 | 0.350 |
| Gravida | 2 (0-6) | 2 (0-9) | 0.940 |
| Parity | 1 (0-3) | 1 (0-8) | 0.697 |
| No. of prior miscarriages | 0 (0-3) | 0 (0-4) | 0.744 |
| Gestational age | 9 (5-15.7) | 9.5 (6-13) | 0.317 |
| Smoking | 5 (7.1%) | 1 (4.2%) | 1.000 |
| TSH | 0.9 (0.3-6.8) | 0.2 (0.01-49.0) | 0.066 |
| fT3 | 4.6 (2.3-5.8) | 4.9 (3.3-6.0) | 0.036 |
| fT4 | 10 (5.1-14) | 11.5 (3.8-24) | 0.022 |
| History of antithyroid therapy | 4 (5.7%) | 7 (29.2%) | 0.005 |
| History of thyroid surgery | - | 3 (12.5%) | 0.015 |
| Family history of thyroid disease | 23 (32.9%) | 5 (20.8%) | 0.266 |
| History of either autoimmune disease | 1 (1.4%) | - | - |

existed in low-risk group.

When the results of the thyroid function tests were evaluated as normal and abnormal, the most statistically significant determinants for abnormal results were history of antithyroid therapy and thyroid surgery (p=0.005, p=0.015, respectively). Table 3 shows the distribution of thyroid functions according to various demographic characteristics of the study group.

## Discussion

Thyroid dysfunction, subclinical or overt, is an important condition and should be diagnosed and treated in a timely fashion during pregnancy because of many proved maternal and fetal adverse outcomes [3-5]. The need to screen thyroid dysfunction in early pregnancy, however, is disputed. While the American Thyroid Association recommends screening and evaluation among women with a high-risk of thyroid disease during pregnancy, many studies now indicate universal screening [15;17-19].

In our study, we screened for thyroid function in first trimester pregnant women and found 12.98% dysfunction in the high-risk group and 5.4% in low risk group. It follows, therefore, that we would miss about one third of women with dysfunction if we tested only high-risk women, as the consensus guidelines recommend [15]. Among the several studies supporting the efficacy of screening all women in early pregnancy, Dosiou et al [17]. reported on the cost-effectiveness of screening all first trimester pregnant women for autoimmune thyroid disease. Vaidya et al.[16] found that one third of women with hypothyroidism would not be diagnosed if only high-risk group is screened, similar to our study, while Chang et al. [22] found that targeted testing would have missed 80.4% of cases. Universal screening was proposed by other authors as well [23;24].

The debate on screening thyroid dysfunction continues, however, as there have also been vigorous studies with wide series that suggest screening only high-risk pregnant women. Miller and Grobman [25]stated that it was premature to recommend universal screening as a result of their study. Testing only high-risk patients remained the recommended strategy in Eastmen's study. [21] Lazarus et al. [20] have reported the screening and treatment of hypothyroid pregnant women to have no effect in improvement of cognitive functions in their children at three years of age.

Since, it is essential to avoid misdiagnosis and inappropriate treatment, so the use of gestational age-specific reference intervals for screening thyroid functions should be preferred [12-14]. Our study was limited insofar as we were unable to obtain reference intervals for our population. Attendance, also is another salient factor for screening. Universal screening might be recommended, but age, place of residence, and education have all been found to influence the program attendance (with younger, less highly educated women living outside of provincial capitals attending less often). [26]

In conclusion, the detection of thyroid dysfunction in early pregnancy is extremely important for both mother and fetus. Despite consensus guidelines recommend screening of only high-risk pregnant women, several studies over the last years have suggested universal screening. The present study offers further evidence in support of this approach. The controversy about whether universal screening or targeting only high-risk cases is the best course of action seems to continue. More studies may be necessary with larger series to establish the optimum strategy.

### *Competing interests*

The authors declare that they have no competing interests.

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